

Τι είναι το μεταβολικό σύνδρομο

***Δούμας Μιχαήλ
Παθολόγος
Β'ΠΠ Κλινική ΑΠΘ***

Δήλωση συμφερόντων

**Δεν υπάρχει καμία σύγκρουση
συμφερόντων σχετικά με αυτήν
την παρουσίαση**

Alternative names



- Metabolic syndrome
- Syndrome X
- Insulin resistance syndrome
- Deadly quartet
- Reaven's syndrome

The WHO Definition : 1998

I- Criteria : [Type 2 diabetes or IGT] * + 2 out of 4 :

- 1- Hypertension
- 2- Blood fat
- 3- Obesity (BMI) **
- 4- micro albuminuria

* In case of normal glucose tolerance , evidence of diminished insulin sensitivity
(by Euglycemic clamp or HOMA)

** Obesity is assessed by BMI or waist/ hip ratio

Definition



Constellation of metabolic abnormalities that confer increased risk of cardiovascular disease(CVD) and diabetes mellitus.



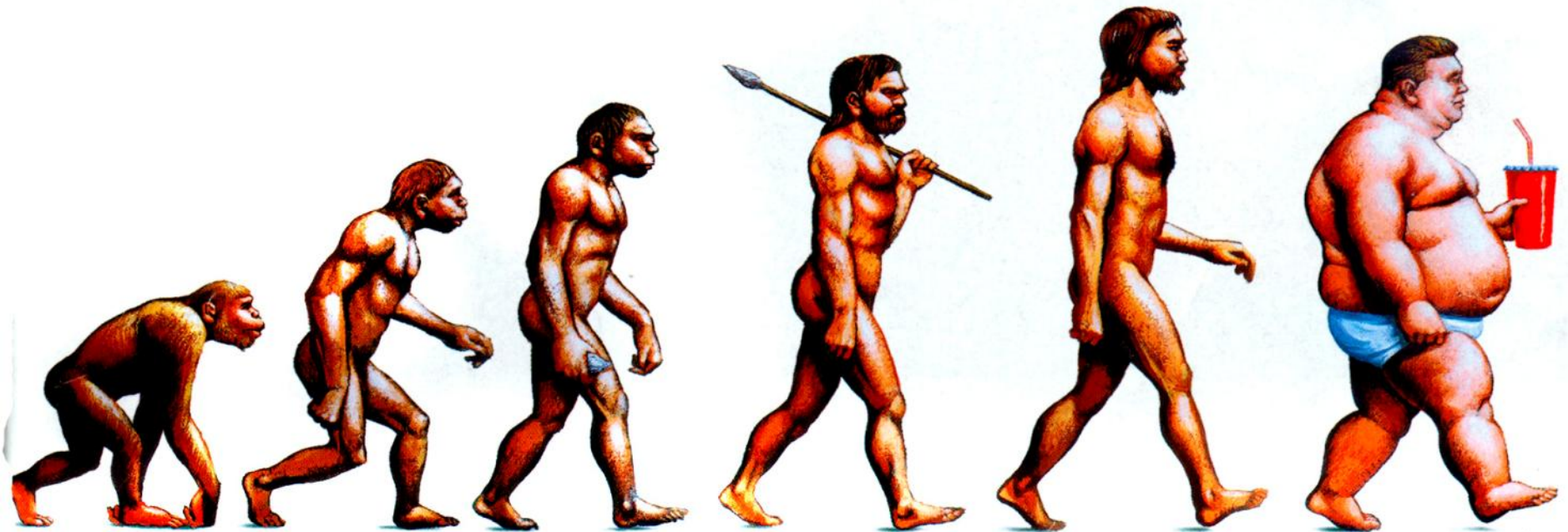
The major features of metabolic syndrome include

- Central obesity
- Hypertriglyceridemia
- Low high density lipoprotein (HDL)
- Hyperglycemia
- Hypertension

The Bottom line....



The shape of things to come



Ορισμοί

Clinical features of metabolic syndrome (NCEP – ATP III)

Feature

Diagnostic criteria

- **Blood pressure** $\geq 130/ 85$ mmHg
 - **Fasting blood sugar** ≥ 110 mg / dl
 - **Waist circumfrence**
 - male >101 cm
 - female >88 cm
 - **Triglycerides** ≥ 150 mg / dl
 - **HDL**
 - male < 50 mg / dl
 - female < 40 mg / dl
-

IDF criteria



1. Waist circumference: ≥ 94 in males ≥ 80 in females
2. Plus two or more of the following
 - a) **Hypertriglyceridemia:** ≥ 150 TG' s or specific medication
 - b) **Low HDL cholesterol:** < 40 (M) and < 50 (F) or specific medication
 - c) **Hypertension:** blood pressure ≥ 130 mm systolic or ≥ 85 mm diastolic or specific medication
 - d) **Fasting plasma glucose:** ≥ 100 mg/dl or specific medication or previously diagnosed T2DM

Cardiometabolic Risk

Ethnic-Specific Values for Waist Circumference: International Diabetes Federation

Country/Ethnic Group		Waist Circumference
United States	Male	102 cm (40 inches)
	Female	88 cm (35 inches)
Europids	Male	94 cm (37 inches)
	Female	80 cm (31 inches)
South Asians and Chinese	Male	90 cm (35 inches)
	Female	80 cm (31 inches)
Japanese	Male	85 cm (33 inches)
	Female	90 cm (35 inches)
Ethnic South and Central Americans	Use South Asian recommendations until more data are available	
Sub-Saharan Africans	Use European data until more data are available	
Eastern Mediterranean and Middle East (Arab) Populations	Use European data until more data are available	

Επιδημιολογία



Επίπτωση του Μεταβολικού Συνδρόμου

Με ΜΣ

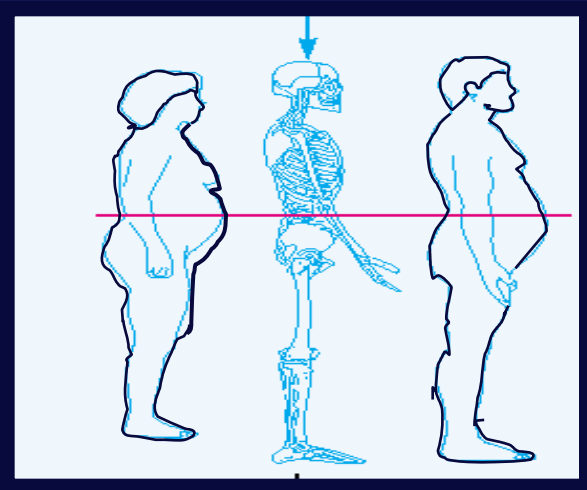
n=2282 19,8%

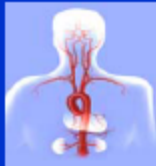
19,8%

80,2%

Χωρίς ΜΣ

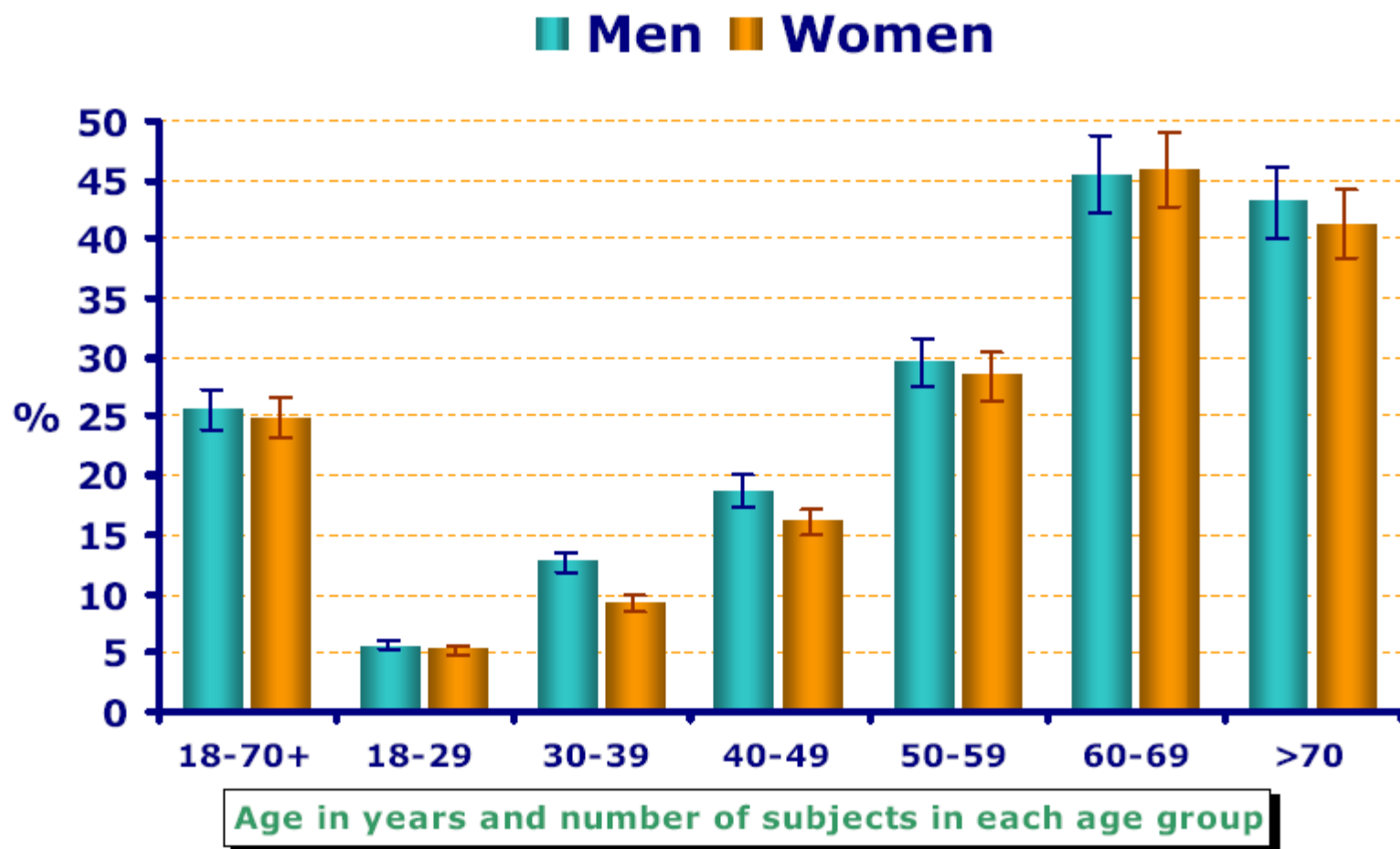
Άνδρες 25.3%
Γυναίκες 14.6%





WATCH METS

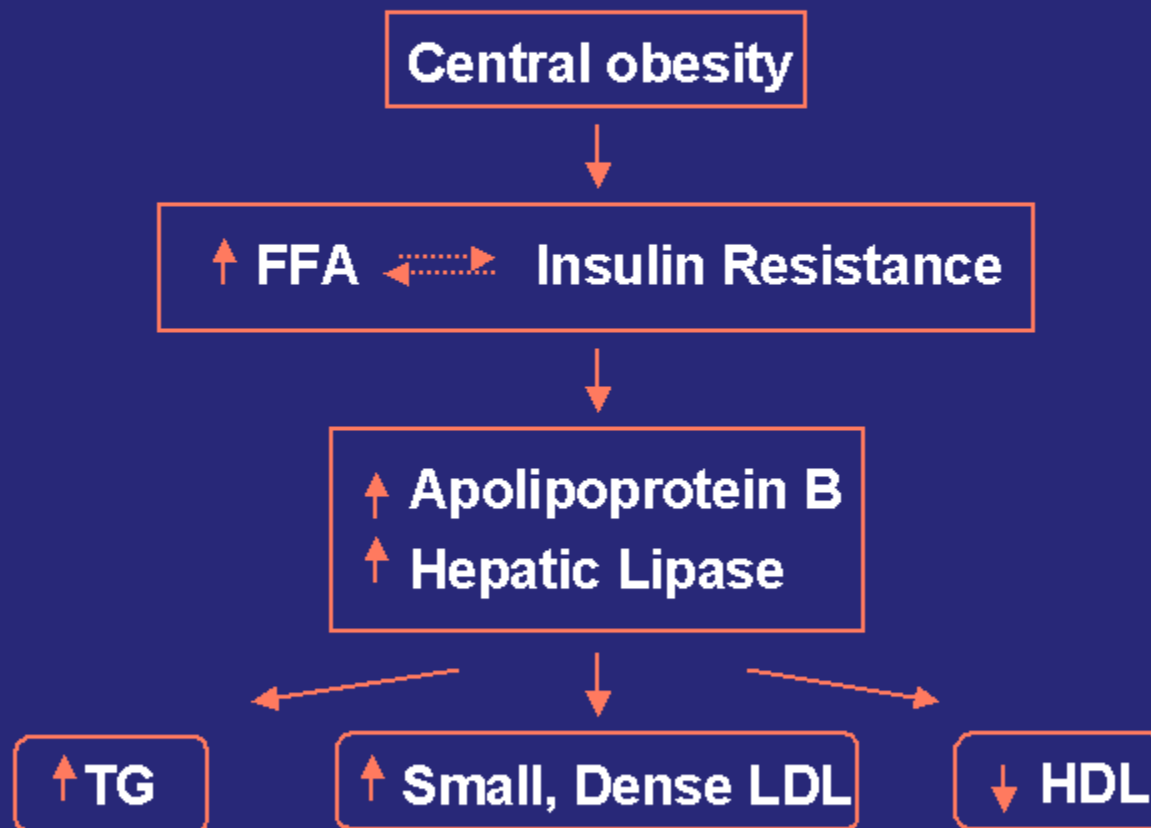
Prevalence of the metabolic syndrome among 8,348 Greek adults aged >18 years, by age and gender.



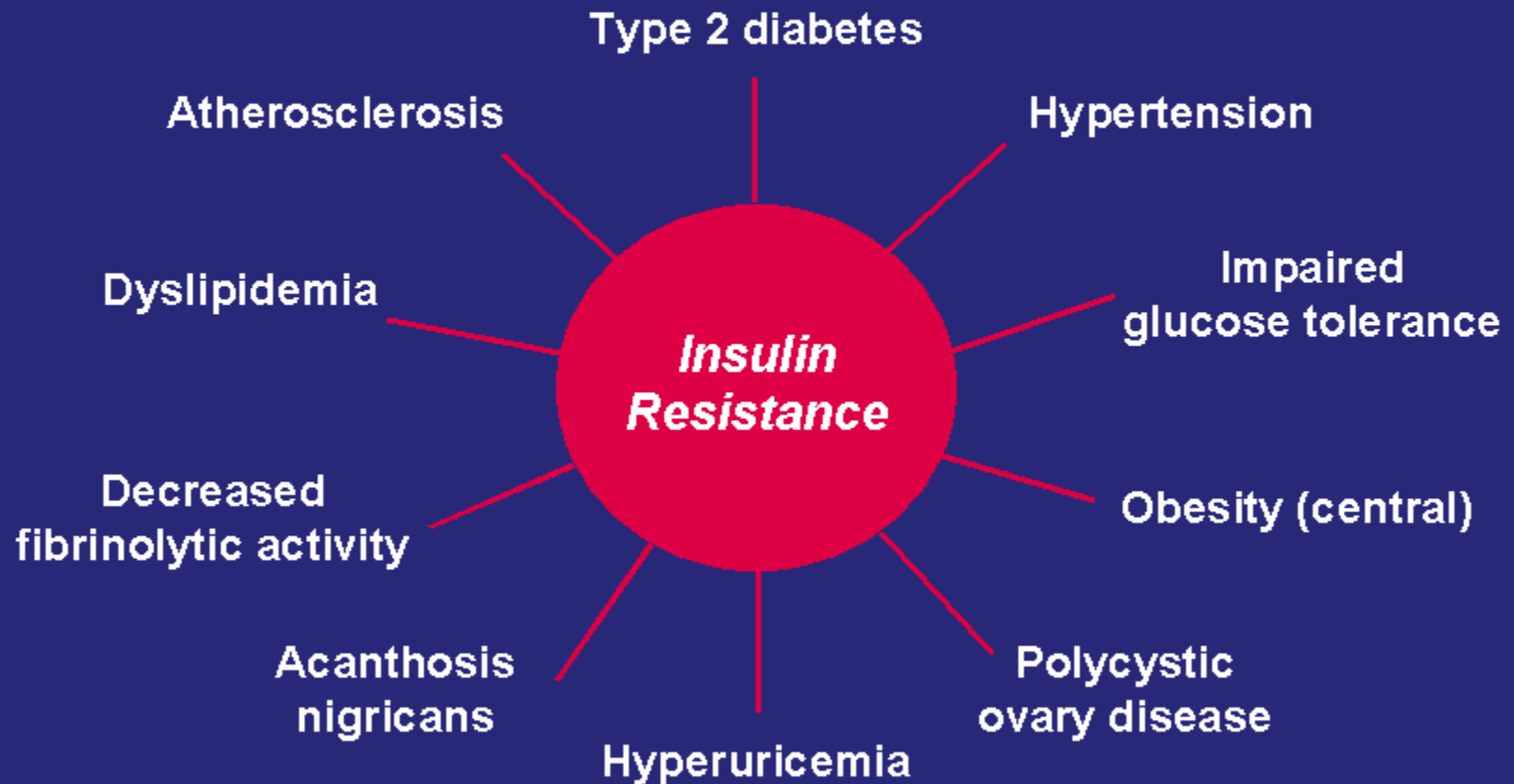
Athyros VG et al. Diabetes Obesity and Metabolism 2005;7:397--405

Παθογενετικοί μηχανισμοί

Relationship Between Obesity and Insulin Resistance and Dyslipidemia

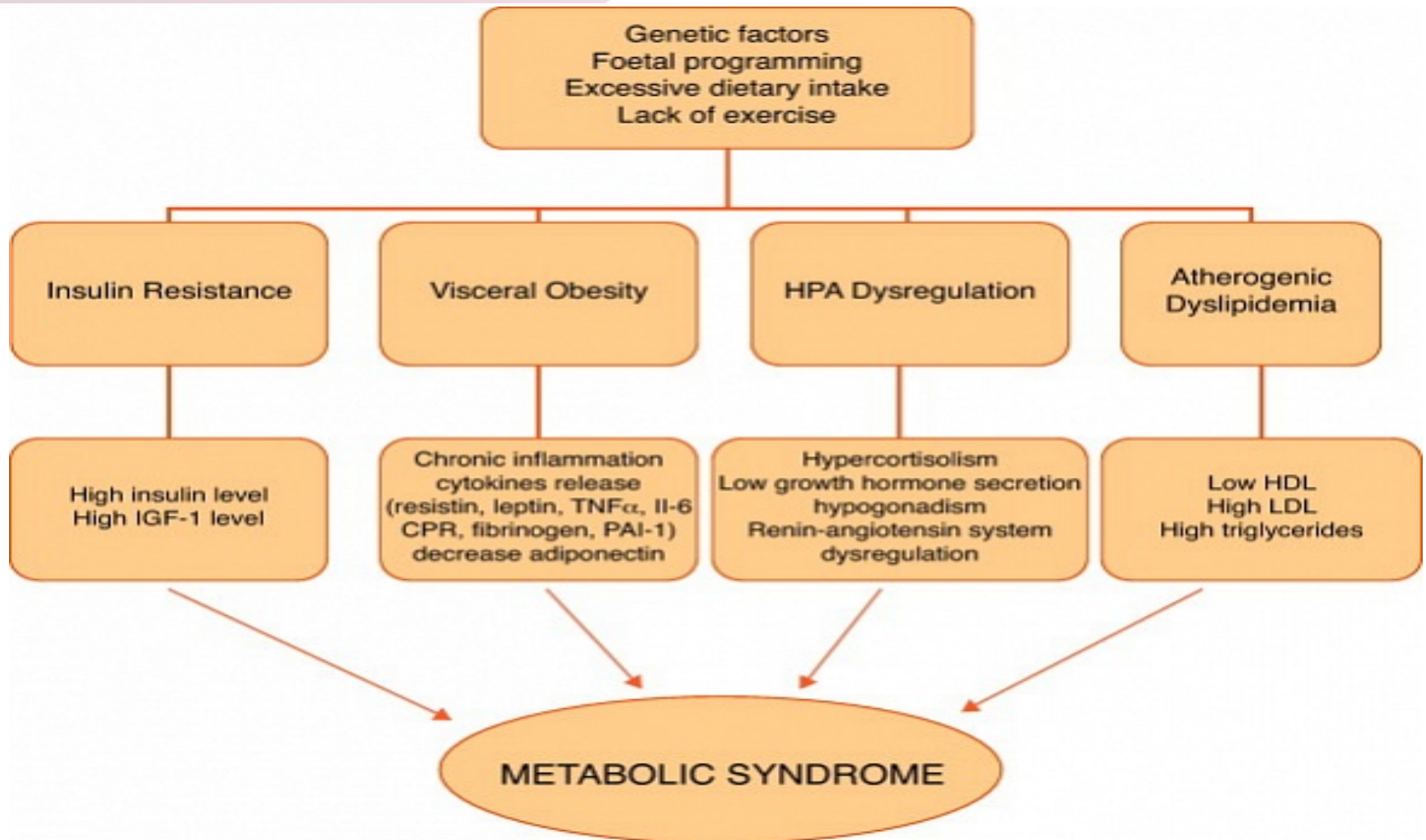


Insulin Resistance: Associated Conditions



Adapted from Consensus Development Conference of the American Diabetes Association. *Diabetes Care*. 1998;21:310-314.

Pathogenesis contd...



Συνοδές καταστάσεις



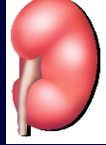
Other associated conditions



- 1) Cardiovascular disease
increased risk for new onset CVD, ischemic stroke, PVD
- 2) Type 2 diabetes mellitus
increased risk by 3-5 folds
- 3) NAFLD and/or NASH
- 4) Hyperuricemia
- 5) PCOS- prevalence 40-50%
- 6) OSA- commonly associated with obesity, HTN & insulin resistance (CPAP improves insulin sensitivity)

Προγνωστική αξία

ESH-ESC 2007: High/Very High Risk Subjects

- ⊘ Συστολική ΑΠ ≥ 180 mmHg και/ή Διαστολική ≥ 110 mmHg
- ⊘ Συστολική ΑΠ > 160 mmHg και/ή Διαστολική < 70 mmHg
- ⊘ 3 Παράγοντες Καρδιαγγειακού Κινδύνου
- ⊘ Σακχαρώδης Διαβήτης
- ⊘ **Μεταβολικό Σύνδρομο**
- ⊘ Ασυμπτωματική Βλάβη Οργάνων-Στόχων
 -  – Υπερτροφία αριστεράς κοιλίας (ΗΚΓ ή U/S)
 -  – Πάχυνση τοιχωμάτων καρωτίδων (U/S)
 - Σκλήρυνση τοιχώματος αρτηριών
 - Μέτρια αύξηση κρεατινίνης
 -  – Μειωμένη κάθαρση κρεατινίνης
 - Μικρολευκωματινουρία ή Πρωτεϊνουρία
- ⊘ Εγκατεστημένη Καρδιαγγειακή ή Νεφρική Νόσος

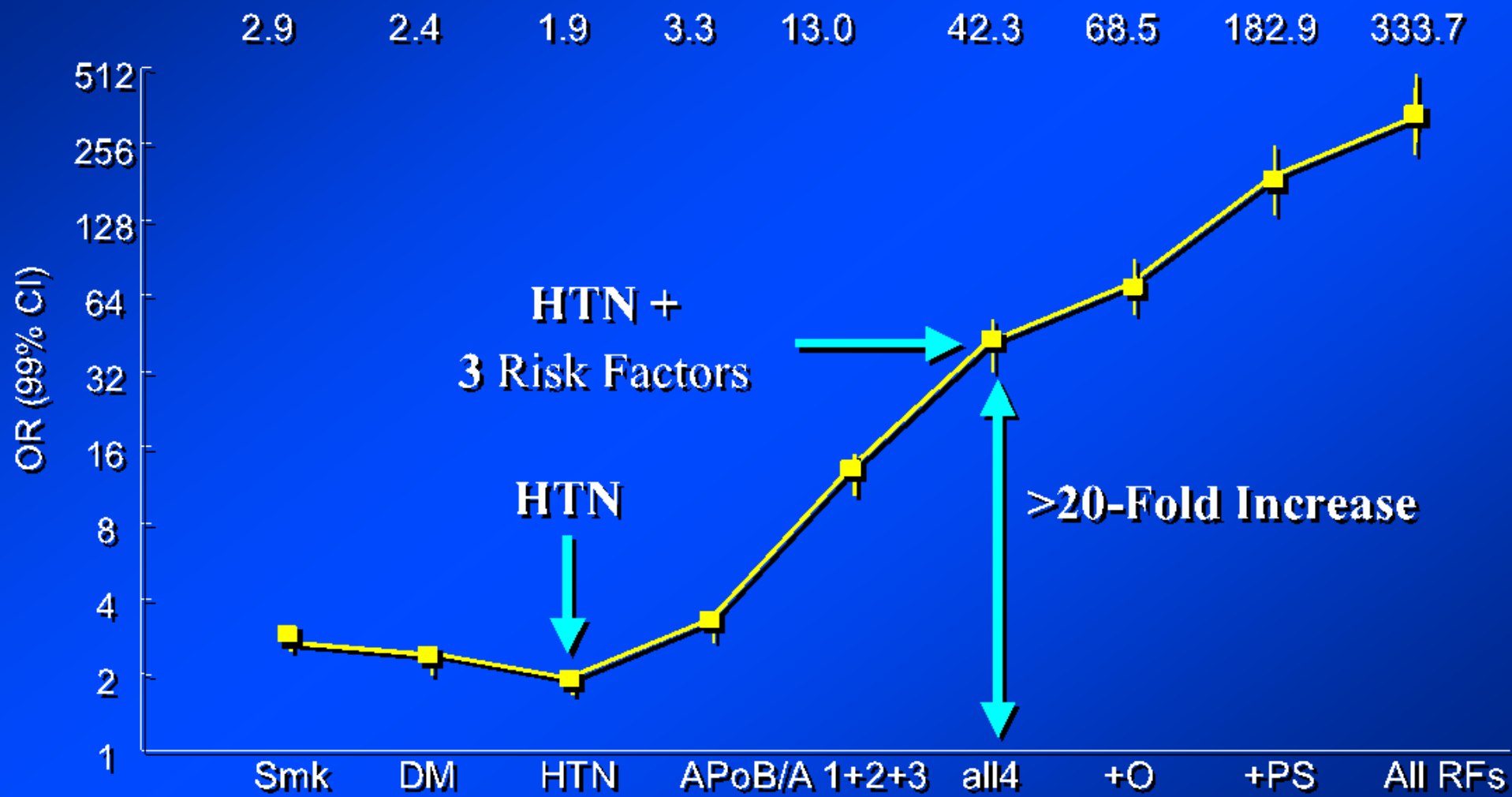
CV risk stratification – 2007 ESC/ESH Guidelines for the Management of Hypertension¹

Other risk factors, OD or Disease	Normal SBP 120-129 or DBP 80-84	High normal SBP 130-139 or DBP 85-89	Grade 1 HT SBP 140-159 or DBP 90-99	Grade 2 HT SBP 160-179 or DBP 100-109	Grade 3 HT SBP \geq 180 or DBP \geq 110
No other risk factors	Average risk	Average risk	Low added risk	Moderate added risk	High added risk
1-2 risk factors	Low added risk	Low added risk	Moderate added risk	Moderate added risk	Very High added risk
3 or more risk factors, MS, OD or Diabetes	Moderate added risk	High added risk	High added risk	High added risk	Very High added risk
Established CV or renal disease	Very High added risk	Very High added risk	Very High added risk	Very High added risk	Very High added risk

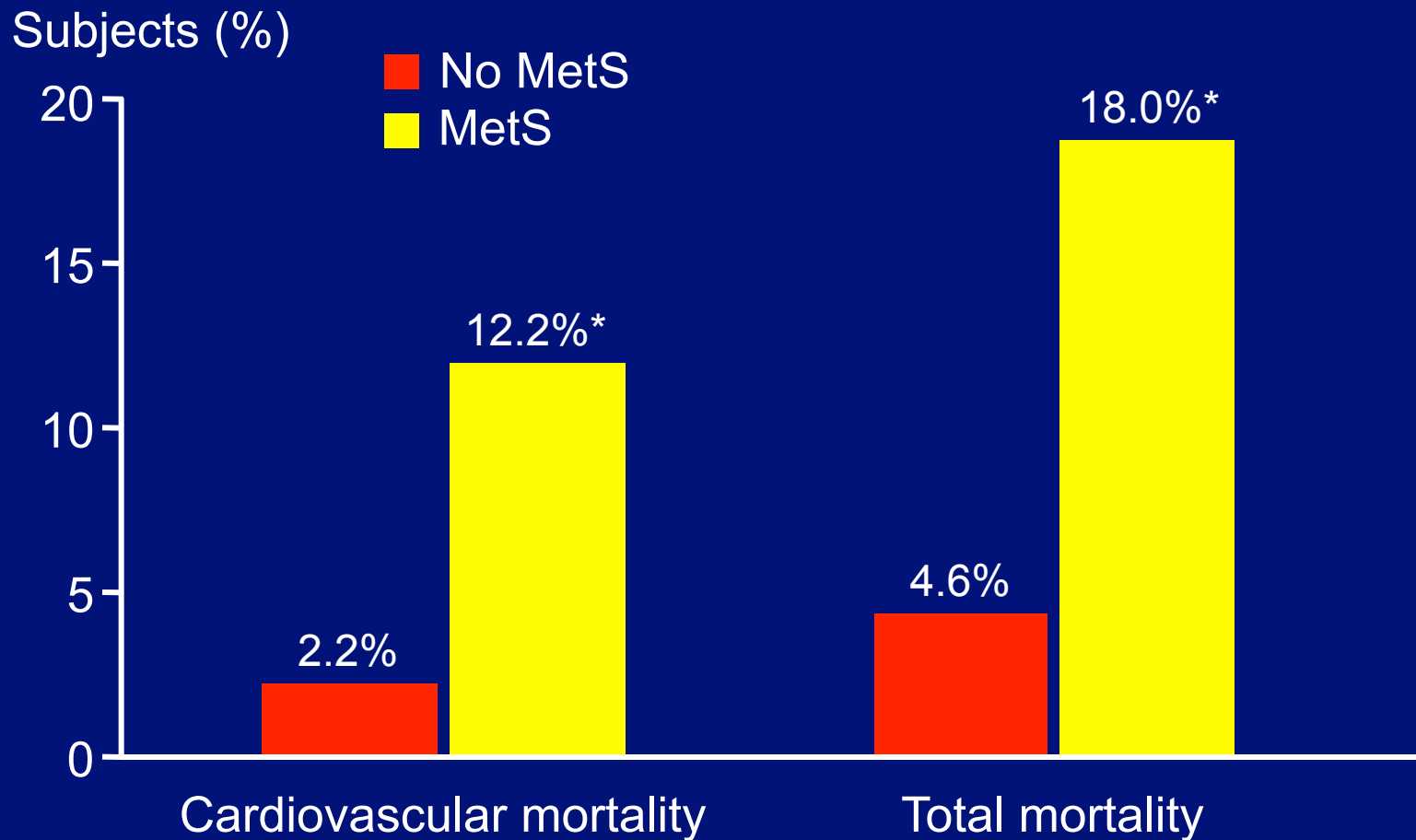
SBP:systolic blood pressure; DBP:diastolic blood pressure; CV: cardiovascular; HT: hypertension.

Low, moderate, high and very high risk refer to 10-year risk of CV fatal or non-fatal event. The term “added” indicates that in all categories risk is greater than average. OD: subclinical organ damage; MS: metabolic syndrome; The dashed line indicates how definition of hypertension may be variable, depending on the level of total CV risk.

INTER-HEART STUDY: CV Events (MI) in Hypertension + Other CV Risk



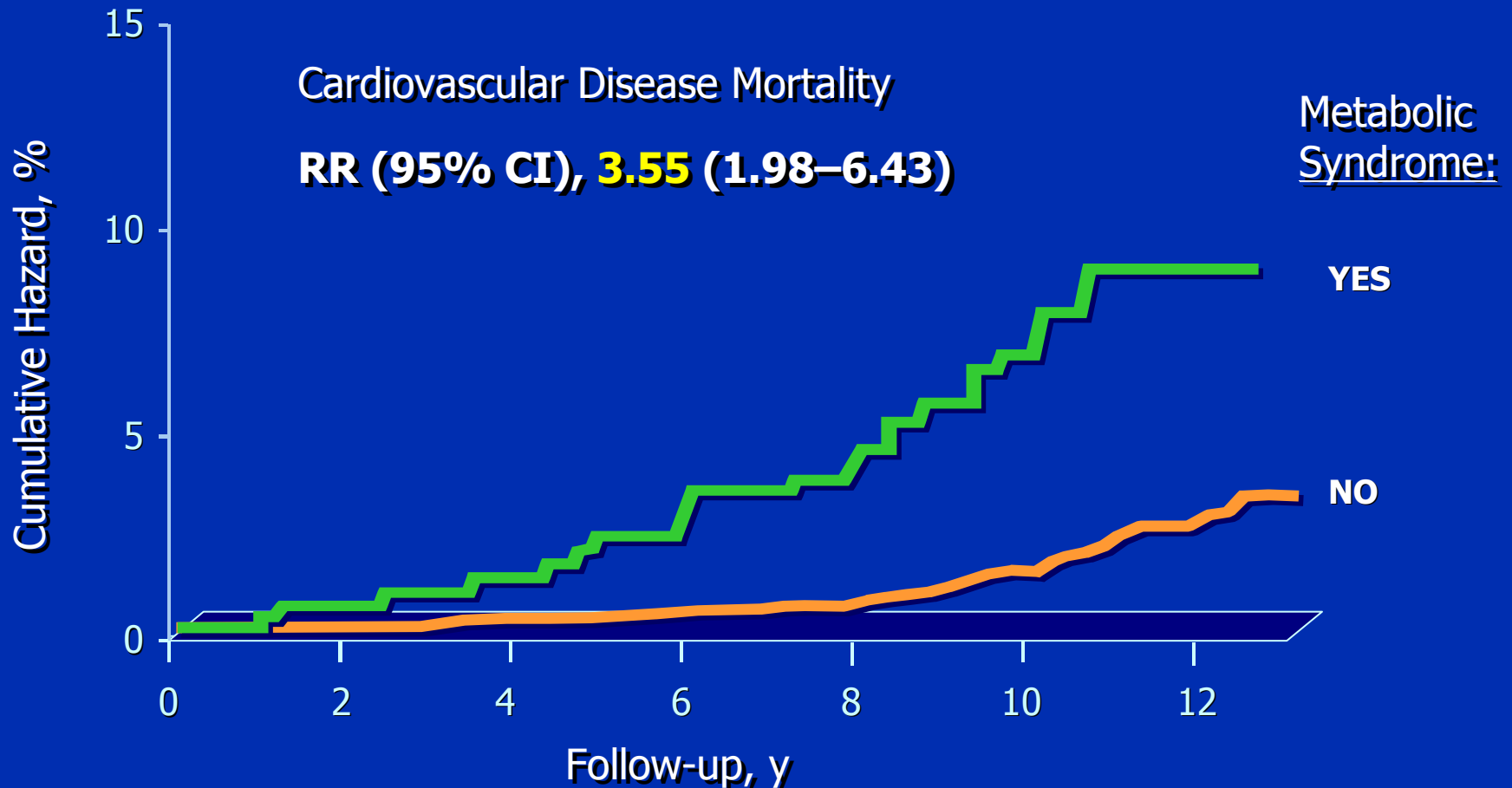
Mortality, especially cardiovascular mortality, is increased in subjects with MetS



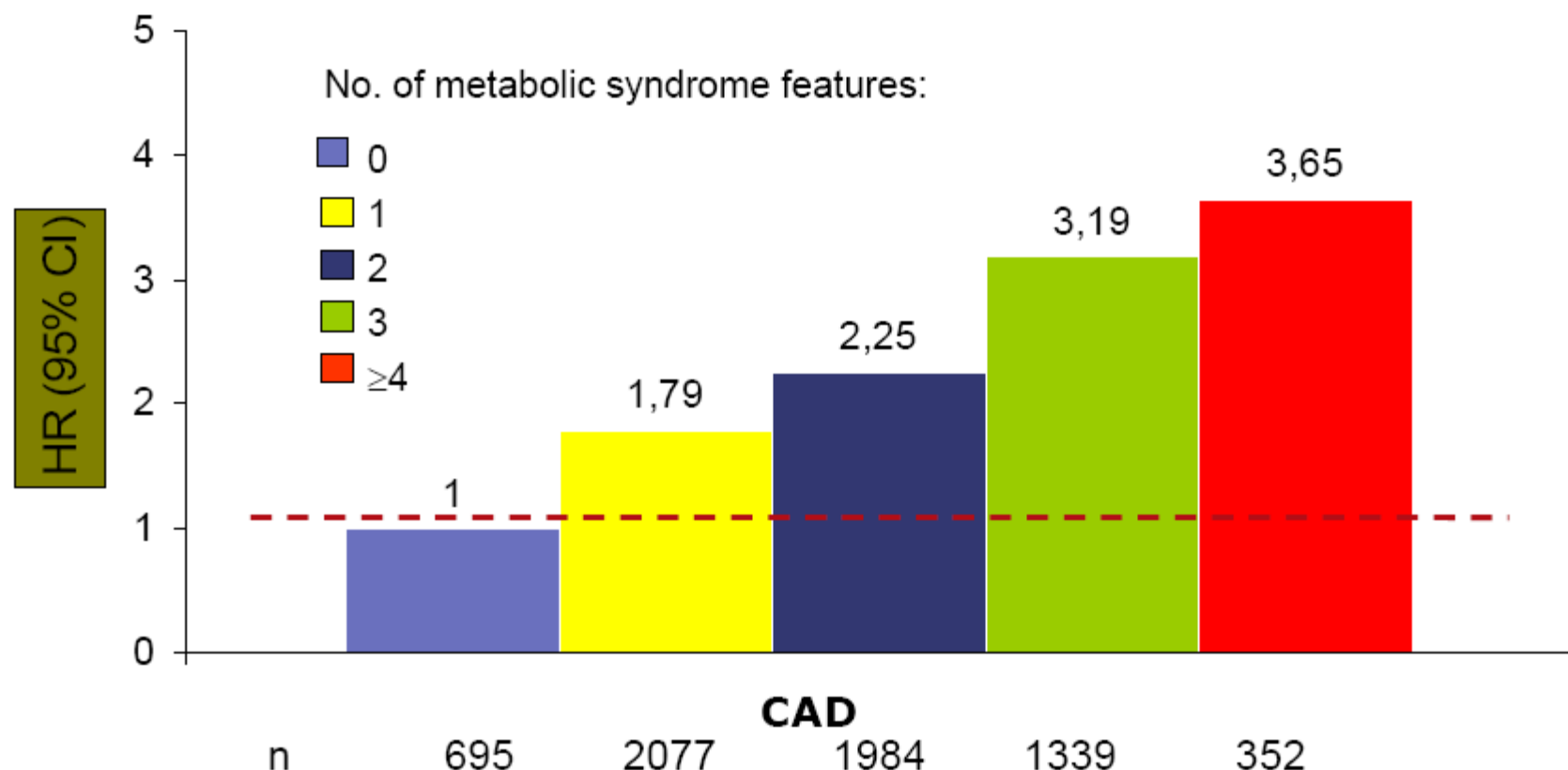
Results of a 7-year follow-up

* $p < 0.001$ vs. subjects without MS

Cardiovascular Disease Mortality Increased in the Metabolic Syndrome: *Kuopio Ischaemic Heart Disease Risk Factor Study*



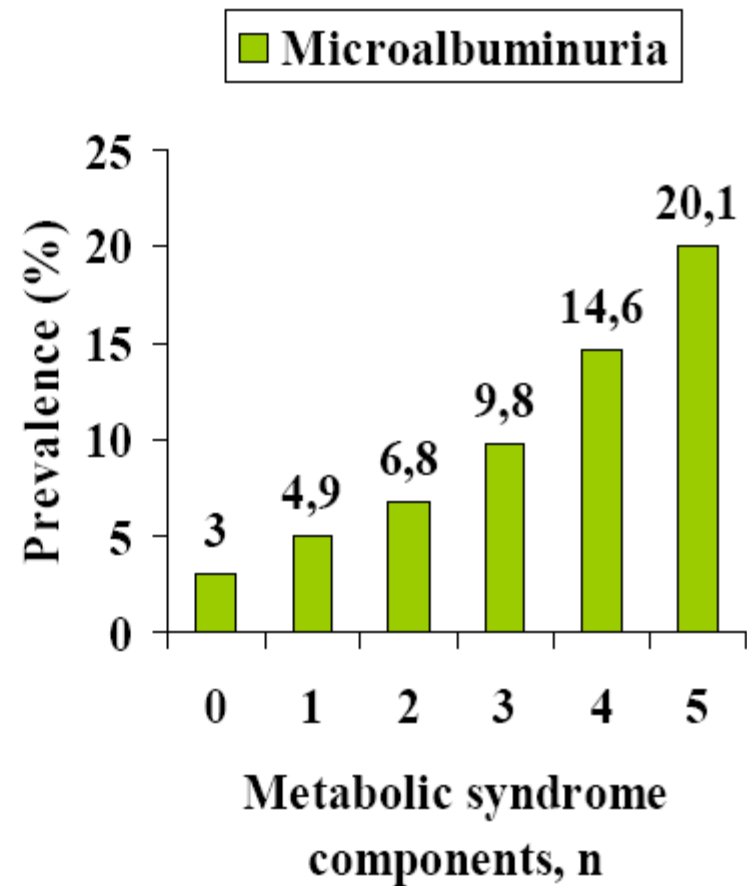
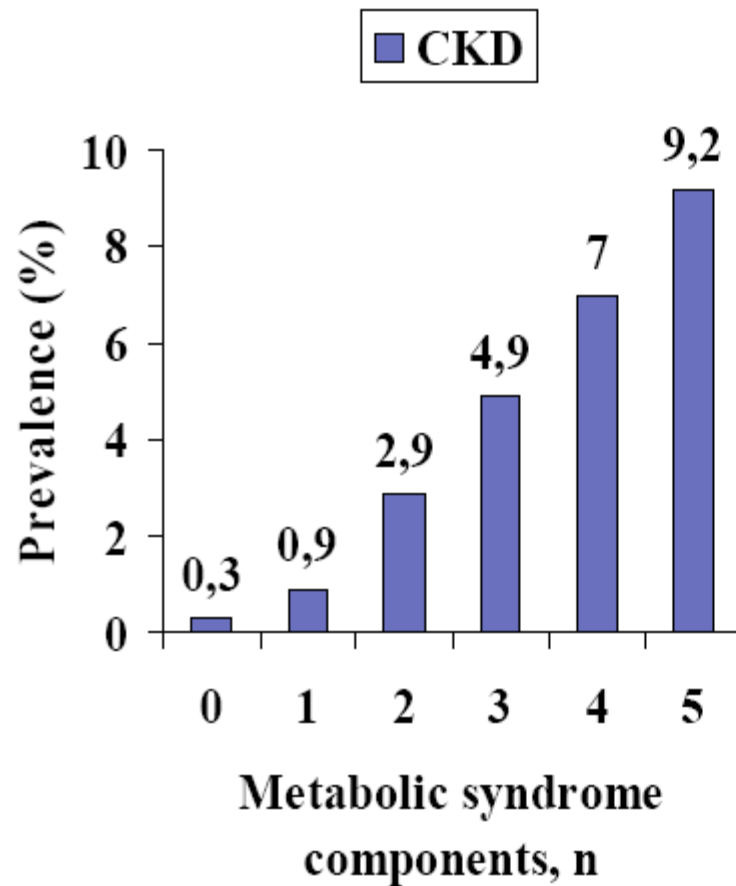
WOSCOPS: CAD Risk Increases With Number of Metabolic Syndrome Criteria



WOSCOPS = West of Scotland Coronary Protection Study; HR = hazard ratio.

Sattar N, et al. *Circulation*. 2003;108:414-419.

Prevalence of CKD (estimated GFR <60 ml/min/1.73m²) and microalbuminuria (urinary albumin-to-creatinine ratio of 30–300 mg/g) by number of MetS components.



Metabolic Syndrome, CVD Events, and Mortality

- *Atherosclerosis Risk in Communities (ARIC) study (12,089 men and women):*
- **11 year follow-up, ATP III MetS associated with 1.5-2-fold greater likelihood of developing CHD and stroke**
- **But MetS did not improve prediction over FRS**
- **(McNeill et al. Diab Care 2005; 28: 385-90)**

Αμφισβήτηση

To be or not to be

The Metabolic Syndrome: Time for a Critical Appraisal

Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes

Does the Metabolic Syndrome Exist?

Ορισμοί

- Πολλοί
- Διαφορές

Αλλά....

Χρήσιμοι μόνο για τις μελέτες !!!

- Γλυκόζη: 101
 - Α.Π.: 136/82
 - Τριγλυκερίδια: 152
 - MS: ΝΑΙ
- Γλυκόζη: 243
 - Α.Π.: 185/112
 - Τριγλυκερίδια: 144
 - MS: ΟΧΙ

Εξαιρετικά ετερογενής ομάδα

- Γυναίκα 36 ετών
- Γλυκόζη: 101
- Α.Π.: 136/82
- Τριγλυκερίδια: 152
- MS: NAI
- CV risk: Χαμηλός
- Άνδρας 68 ετών
- Γλυκόζη: 243
- Α.Π.: 185/112
- HDL: 28
- MS: NAI
- CV risk: Πολύ υψηλός

Prediction of CV or All-Cause by MS Components and Their Combinations

Type of Model	-2 Log L	<u>CV Mortality</u>		<u>All- Cause Mortality</u>		
		LRT	<i>P</i>	-2 Log L	LRT	<i>P</i>
Waist circumference	581.029	0.341	0.5593	2177.910	1.189	0.2755
Triglycerides	580.508	0.862	0.3532	2175.603	3.496	0.0615
HDL cholesterol	581.369	0.001	0.9748	2178.431	0.668	0.4137
Glycemia	573.586	7.784	0.0053	2174.630	4.469	0.0345
BP	576.555	4.815	0.0282	2174.450	4.469	0.0311

MS or not ?



“The Road Not Taken” by Robert Frost

Χρησιμότητα

- ❌ Πιθανότητα ύπαρξης πολλών παραγόντων σε «υποκλινικά» όρια
- ❌ Αρτηριακή πίεση: 138/88 mmHg
- ❌ Γλυκόζη: 117 mg/dl
- ❌ Προσοχή στην αντιμετώπιση πολλών παραγόντων κινδύνου ταυτόχρονα

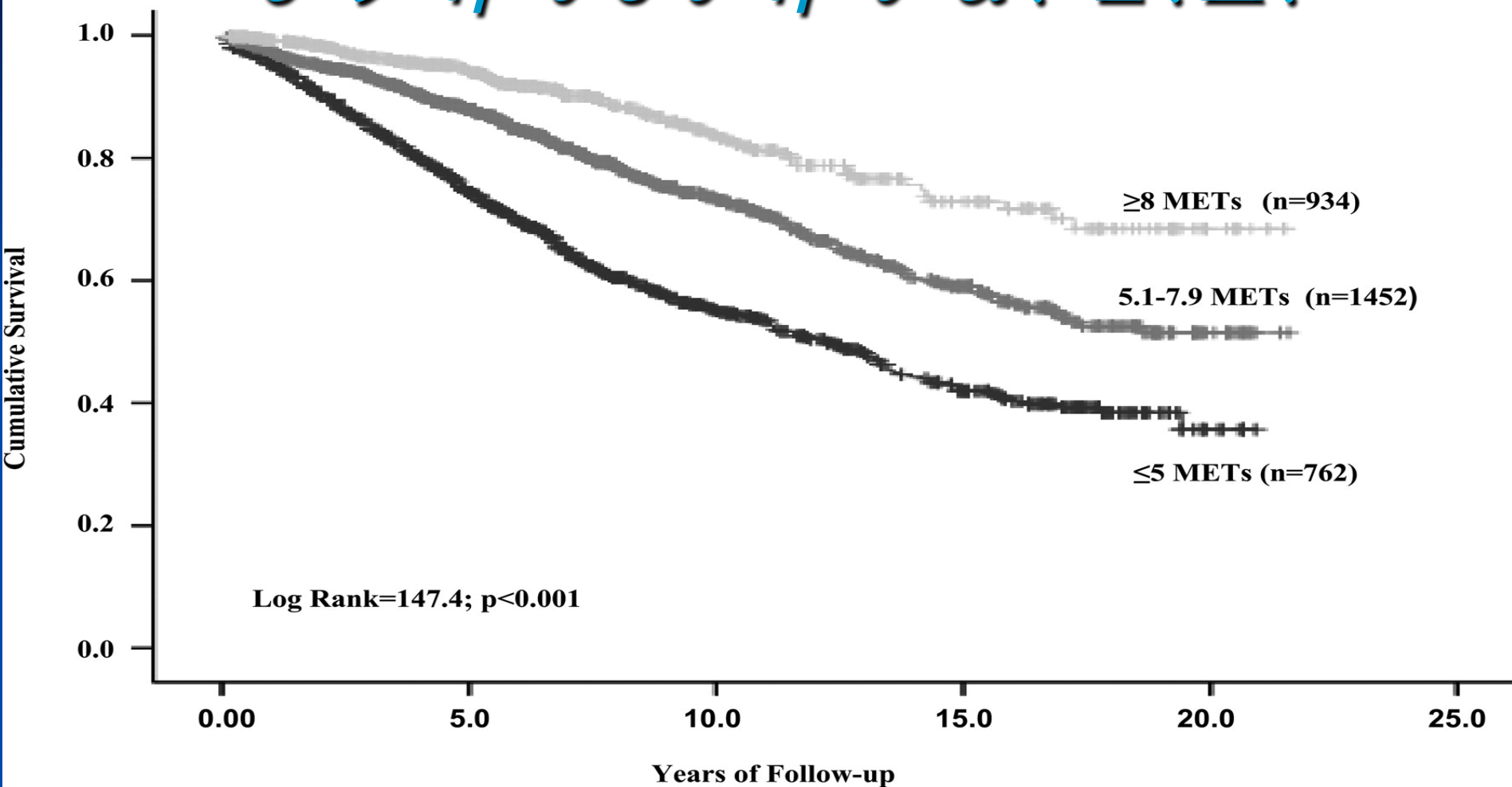
Θεραπεία

Αλλαγή τρόπου ζωής

- Απώλεια βάρους
- Υποθερμιδική δίαιτα
- Δίαιτα σακχαρώδη διαβήτη
- Άλιπος δίαιτα
- Περιορισμός άλατος

- Άσκηση

Άσκηση και θνητότητα: Σ.Δ.



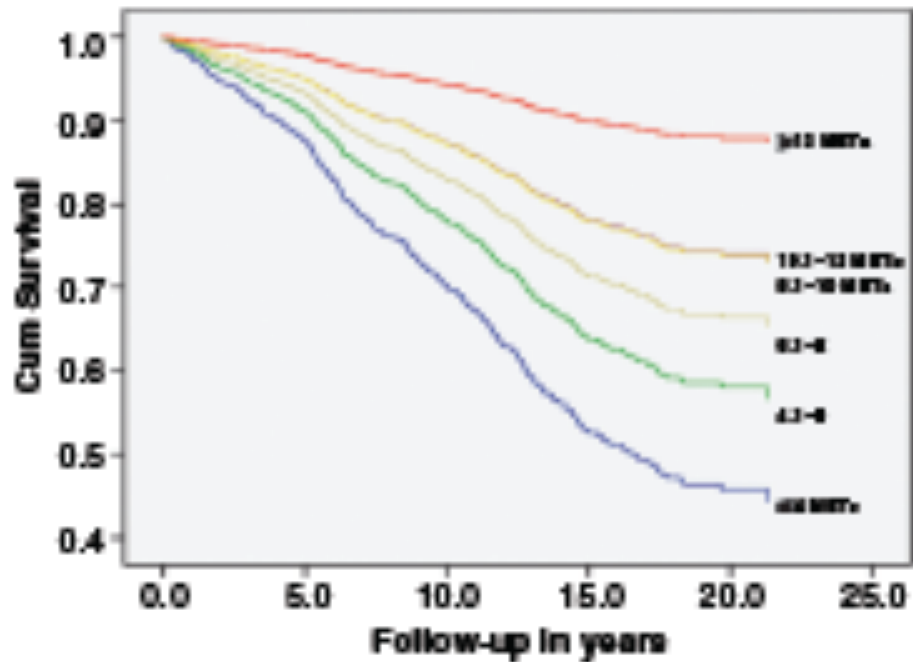
No. of Cumulative Events

≤ 5 METs	218	340	386	394
5.1-7.9 METs	156	270	325	339
≥ 8 METs	37	71	87	90

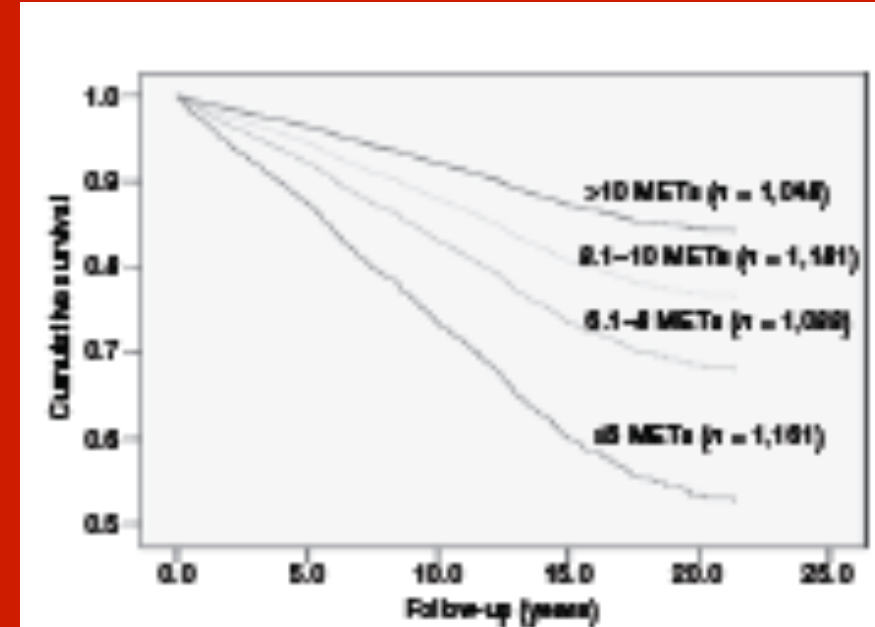
**Kokkinos
Diab Care 2009**

Άσκηση και θνητότητα

High-normal blood pressure



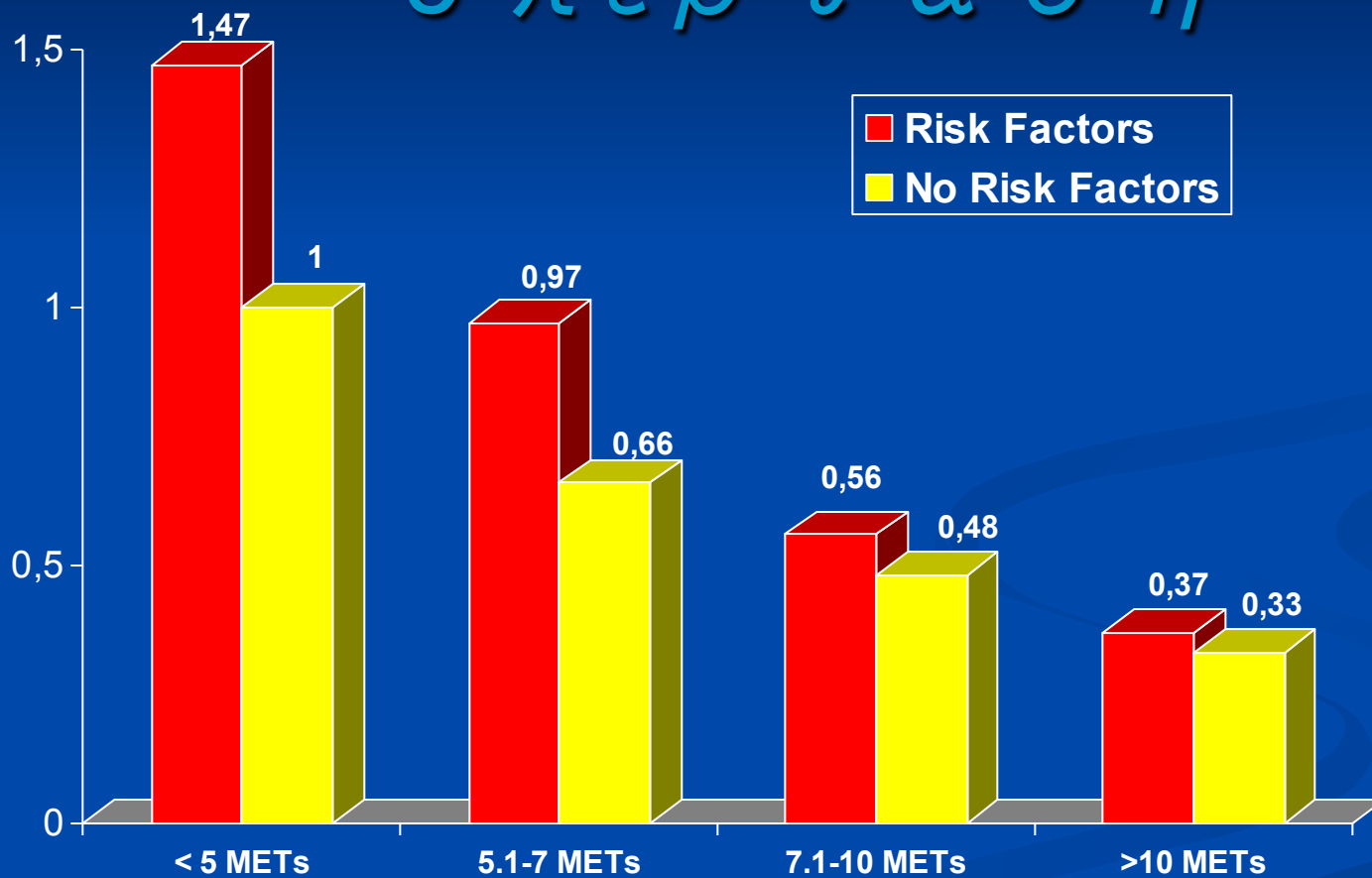
Prehypertension



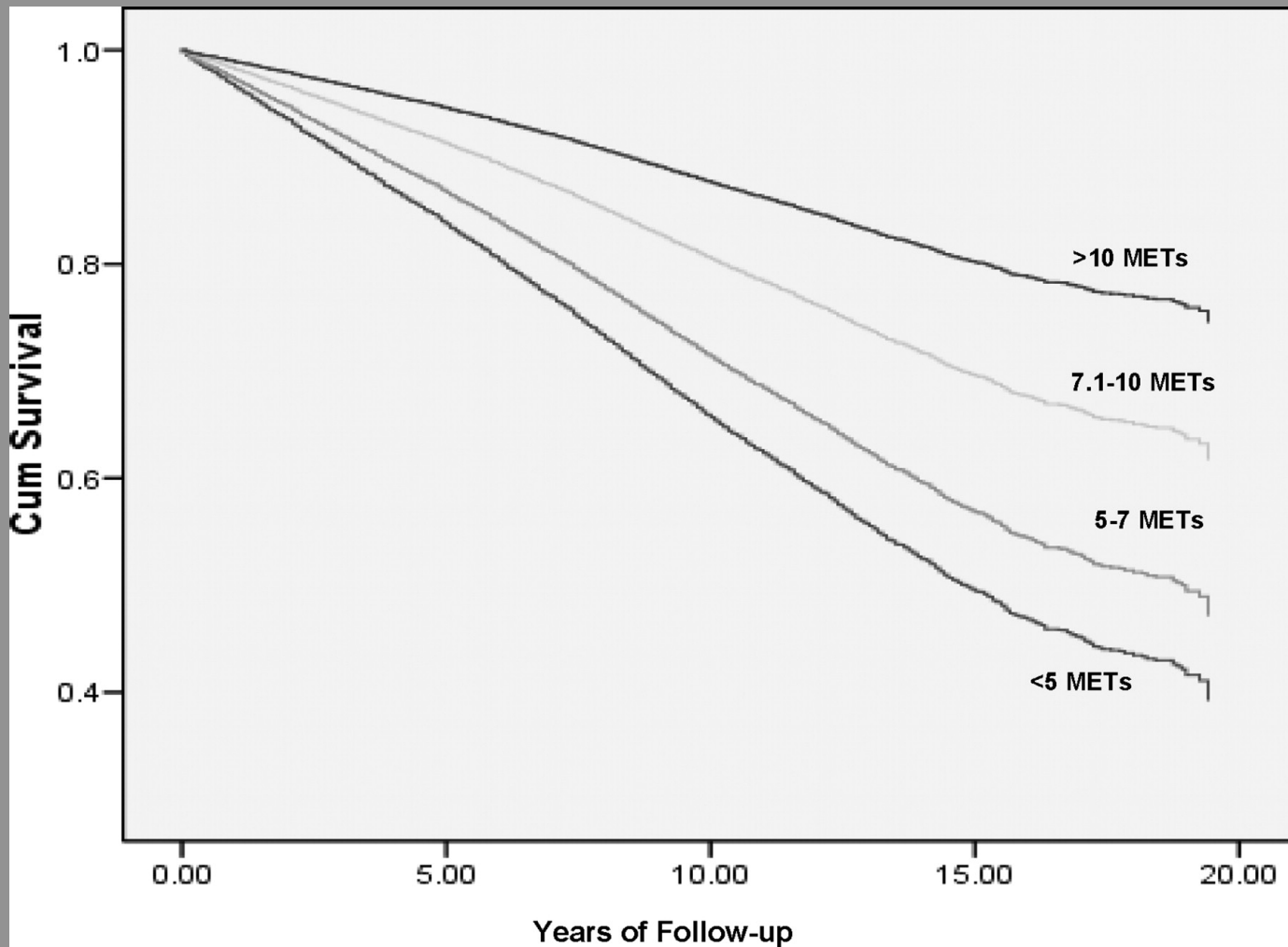
Kokkinos, Blood Pressure 2009

Kokkinos, Amer J Hypertens 2009

Άσκηση και
θνητότητα
υπέρταση



Άσκηση και θνητότητα



Kokkinos, P. et al. *Circulation* 2008;117:614-622



Φάρμακα ???

- Μετφορμίνη, Γλιταζόνες
- Φιμπράτες, Νιασίνη, Ω-3 λιπαρά
- Αντιαιμοπεταλιακά
- Αντιυπερτασικά φάρμακα

Μεταβολικό σύνδρομο – ESH 2008

Recommended

Non-pharmacologic treatment

First choice: ACEi or ARB

Second choice: Ccb or b-blocker (vasodilating)

Observations

Diuretics should be avoided in monotherapy or high dose

B-blockers should be avoided if not indicated

Combination of diuretics+b-blockers should be avoided

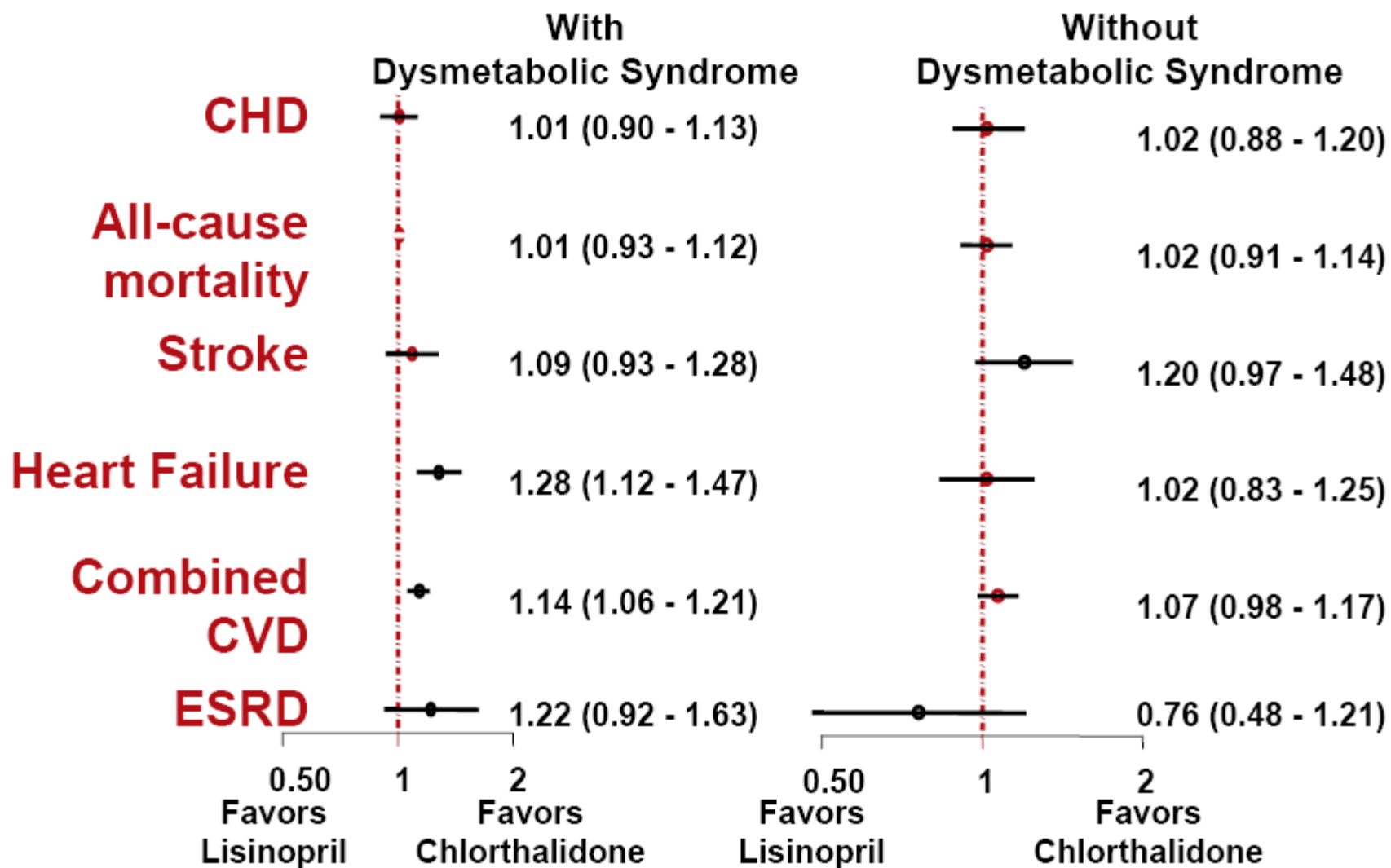
IN GOD WE
TRUST

THE REST MUST SHOW
DATA...



Lisinopril/Chlorthalidone

Relative Risk and 95% Confidence Intervals



Ευχαριστώ πολύ για την προσοχή σας ...



Historical Context :

- 250 ys ago , Morgagni : associated visceral ob.
 - HTN - atherosclerosis - uric acid
 - obstructive sleep apnea.
- 1947 Vague (France): Android obesity.
- 1960 : Plurimetabolic Syndrome
 - (ob+ diab + bld lipids + risk CHD.)
- 1980 : Syndrome X : glucose & insulin metab +
 - + obesity + HT + dyslipidemia
 - Reaven : Insulin sensitivity - risk CHD -
 - insulin resistance

The NCEP metabolic syndrome: prevalence in the NHANES III study

- Abdominal obesity 39%
- Hypertriglyceridaemia 30%
- Low HDL-cholesterol 37%
- High blood pressure or medication use 34%
- High fasting glucose or medication use 13%
 - ≥ 1 metabolic abnormality: 71%
 - ≥ 2 metabolic abnormalities: 44%
 - ≥ 3 metabolic abnormalities: 24%